

paragraph, because the claims define nucleic acids used in the claimed methods by percent identity. Each of the rejections will be addressed below.

New Matter Rejections

Claims 1, 24, 35, 40, and 45 stand rejected for reference to modulation of seed "oil content", which the Examiner alleges is not disclosed in the application as filed. Applicants acknowledge that the previous response identifies support for claim 45 that refers to "fatty acid content". In fact, however, the specification, as filed, is replete with references to alteration of seed "oil content". For example, in the Summary of the Invention, at page 3, lines 10-14, the use of ADC to "increase protein content, carbohydrate content or oil content" is discussed. Similarly, claim 3, as originally filed, specifically recites increased oil content. In light of the clear discussion of modulation of oil content using the claimed methods, the rejection for alleged new matter is improper and should be withdrawn.

Rejections under 35 U.S.C. § 112, first and second paragraphs

Claims 1-4, 6-14, 16-25, 27-35, 37, 40, and 45 stand rejected because the claims recite polypeptides comprising an AP2 domain at least about 35% identical to SEQ ID NOs: 4 or 5. The Examiner alleges that, using the present application which refers to use of the BLAST program set at "standard parameters" (*see*, page 7, lines 13-16), one of skill would not understand the metes and bounds of the present invention. The Examiner next alleges that using only the functional definition of the nucleic acids used in the claimed methods (*i.e.* they encode polypeptides that modulate seed mass or oil content), one of skill cannot predict the structure of the nucleic acids that are useful in the claimed methods. As explained in the attached declaration of Dr. Nickolai Alexandrov, using the present application and common knowledge available at the time of the application, one of ordinary skill could have identified nucleic sequences as defined in the claims. Thus, one of skill could have readily prepared appropriate nucleic acid constructs and practiced the claimed methods at the time of the invention.

As explained Dr. Alexandrov, as of the filing date of June 20, 1997, one of ordinary skill in the art would have been enabled to use a sequence alignment computer

algorithm, such as BLAST, to determine the percent sequence identity between two polypeptide or nucleotide sequences.

As of the filing date, version 1.4 of the BLAST sequence alignment computer algorithm was available via email (*blast@ncbi.nlm.nih.gov*). Thus, any email user could access the BLAST sequence alignment computer algorithm at the National Center for Biotechnology Information (NCBI). The BLAST algorithm is based on the statistical methods described by Altschul, J. Mol Biol. 219:555-65 (1991) and Altschul, J. Mol. Evol. 36:290-300 (1993). Therefore, the results of a sequence comparison using the BLAST algorithm available at the email address above (*blast@ncbi.nlm.nih.gov*) as of June 20, 1997 would be identical to results from any other available source of the BLAST algorithm set to the same parameter specifications. The operation and default parameters of BLAST v1.4 were available by email (type "help" in the body of the message and mail to: *blast@ncbi.nlm.nih.gov*) as of June 20, 1997. Currently the BLAST v1.4 manual is available on the internet (e.g., <http://blast.wustl.edu/blast-1.4/blast1.pdf>) or may be accessed by email by typing "help" in the body of the message and e-mailing to: <ftp://ncbi.nlm.nih.gov/blast/documents/blemail.txt>). The manual as available on the internet is attached as Exhibit B to Dr. Alexandrov's declaration. The default (i.e. standard) parameters disclosed in the manual include the default scoring matrix for the blastp function (BLOSUM62), the expect default (10), and the cutoff or "S" parameter (calculated from the expect parameter). BLAST v1.4 did not use a filter to reduce non-specific, low-complexity sequences. BLAST v1.4 does not allow for gaps within sequences.

Exhibit C of the declaration provides a typical comparison using BLAST v1.4 using the above-described standard parameters to determine percent identity between SEQ ID NO:4, i.e. one of the AP2 domains disclosed in the present application. and the "nr" database. The "Ungapped BLAST search" (i.e. BLAST v1.4) was chosen from a NCBI web page (<http://www.ncbi.nlm.nih.gov/BLAST/>). From the "Advanced BLAST" page (<http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-blast?Jform=1>), the "blastp" program was selected to compare a polypeptide sequence to an polypeptide database. Default parameters were set for all parameters except "filter," which was set to "none." The polypeptide query sequence of SEQ ID NO:4 was entered into the data entry box and the query was submitted.

The resulting blastp results display a number of polypeptides that are related to SEQ ID. NO:4 and displays their sequence identity. For instance, in the first sequence displayed, one subsequence of the "FLORAL HOMEOTIC PROTEIN APETALA2" was 100% identical with SEQ ID NO:4. In general, at least one alignment is displayed for each related protein, including percentage identity relative to the queried polypeptide sequence.

Because BLAST v1.4 does not use a gapping function when comparing sequences, BLAST v1.4 may break a particular sequence into separate parts and display an alignment and separate percent identity for each part of the sequence. If this occurs, percent identity to the entire query sequence can be calculated by weight averaging the percent identity for each part. For example, if the entire query sequence is divided into two parts by the BLAST algorithm such that three quarters of the entire query sequence is 60% identical to the target sequence and the other one quarter of the query is 20% identical to the target sequence, then the weighted average of the sequence identity would be 50% ($0.75 \times 60\% + 0.25 \times 20\% = 50\%$).


Exhibit C demonstrates the basic steps of determining sequence identity between two protein sequences using BLAST v1.4. These steps for sequence comparison were known to those of ordinary skill in the art at the filing date of Application No. 08/879,827. Therefore, Dr. Alexadrov concludes that the disclosure of a query sequence, *e.g.*, an AP2 domain, and a stated percent identity would have enabled one of ordinary skill in the art to determine whether other polypeptide sequences were at least as identical to the query sequence as the stated percent identity.

In light of the above, applicants believe one of skill could have readily prepared nucleic acids recited in the claims and practiced the claimed methods without undue experimentation. The rejection is therefore improper and should be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is urged. If a telephone conference would aid in the prosecution of this case in any way, the Examiner is invited to call the undersigned at 415-576-0200.

Respectfully submitted,


Kevin Bashian
Reg. No. 34,774

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
KLB
SF 1035398 v1